

16 JUL 2019

Discuss Seresto Incident Profile

**Bayer Participants:**

Jennifer Schofield

Will Heeb (by phone)

Daniel Keil (by phone)

Robert Zolynas (by phone)

**SafetyCall International (SCI) Participants:**

Rick Kingston

Ahna Brutlag (by phone)

**EPA Participants:**

Catherine Aubee

Melanie Biscoe

Julie Breeden-Alemi

Cathryn Britton

Donna Davis

Venus Eagle

Vanessa Emerson

Beth Fertich

Rachel Fletcher

Letu Kassa

Bob Miller

Colleen Rossmeisl

Charles "Billy" Smith

Steven Snyderman

Shana Recore (by phone)

**Introductions**

**Focus:**

- 1) Provide a larger EPA audience for BAH to share trend and incident data (previously shared on 02MAY2019)
- 2) Open broader discussion of some of the common observations coming forward – review and discuss trends observed by EPA

A discussion of the Seresto adverse event (AE) profile (based on BAH update chart) was presented by Rick Kingston of SCI: Weber effect = initial high number of calls; once the marketplace becomes familiar with the product, reporting decreases; numbers reach a plateau, allowing for benchmarking; familiarity with the product = stabilization of reporting; peaks may then signal an issue (e.g., manufacturing, introduction of a new product for which there may be toxicological synergy).

In response to EPA inquiry, BAH noted that the Seresto AE chart as presented is not broken down by correlation (submission of correlation not required); despite this, rates are low from a big picture perspective:

**Ex. 4 CBI**

There was a brief discussion of distribution versus dispensing. BAH noted they are not at liberty to disclose dispensing information.

EPA asked why the rate is evaluated per 10,000 collars? Kingston responded that an incident rate of 1 in 10,000 for a specific effect is commonly used as a trigger to consider a review.

There was confirmation of the change in manner of interpretation/categorization as discussed with EPA and initiated in July of 2018. It was noted that Bayer's original coding practices were very conservative (i.e., events coded at the highest causality category) and that the change resulted in more appropriate categorization of events. It was further noted that Bayer captures and reports every call that comes in regardless of potential (lack of) causality.

EPA indicated a desire to understand what information BAH is collecting. BAH explained that reporting must be sufficient to address global requirements; all information is compiled locally as well as globally; evaluated for signal detection; cases are reviewed twice by veterinary professionals after entry.

Catherine Aube noted that few narratives are submitted directly to EPA; those that do come through are commonly seizures/convulsions.

BAH reviewed evaluation and confirmation of signals including the most recent evaluation of compiled 2018 data by the Local Safety Management Team in Q2.

Seizures and convulsions were briefly discussed with a notation by BAH that seizure rates for dogs wearing Seresto were low compared to the rate described in the literature for the general dog population.

BAH has evaluated adverse events against all aspects of signalment – no patterns identified (breed, age, weight/collar size); rates in cats and dogs are relatively similar.

Colleen Rossmeisl of EPA asked if there was anything BAH felt should be communicated to the medical community regarding the safety of the collar. BAH responded there was not. BAH is committed to the safety of their products and feels the evaluations conducted (and those which are continually ongoing) are robust. BAH's policy around Binding Safety Information ensures critical language is included on product labels globally.

SCI further noted that there was nothing of concern regarding systemic signs from their perspective with respect to human exposures or the sub-set of animal D-As and D-Bs involving systemic signs collected from 2013-2015 that they investigated in an independent audit.

EPA commented on language included in the German label as related to neurologic signs. BAH indicated they were unfamiliar with the exact language included in the German label, but that such information may have been requested by the German authority (specific country requests are not uncommon based on EU approval practices). BAH confirmed that if a medical concern is noted, Binding Safety Information practices would require addition of appropriate language to all labels globally.

BAH noted that there is often an inability to compare AE data between products. However, BAH has three similar EPA registered products (Advantage, K9 Advantix, Seresto) which may be evaluated to provide perspective. Based on a comparison of the adverse event profile for K9 Advantix and Seresto, the Seresto trend is normalizing and is now on par with the safety profile of K9 Advantix.

The meeting was cordially concluded. No immediate actions requested.